REMARKS

In the Office Action under reply, claims 1 and 3-21 are pending. Claims 8-11 have been withdrawn from consideration as being drawn to non-elected subject matter. Claims 1, 3-5, 12 and 18-21 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enabling disclosure in the specification. Claims 13-17 have been objected to as dependent upon a rejected base claim but are indicated as otherwise allowable if rewritten in independent form.

Additionally the Examiner has objected to claim 12 as being of improper dependent form and reminded the Applicants of the need to submit copies of the references submitted with the IDS of 6/15/04.

In the present amendment, claims 1 and 13-17 have been amended and claims 6-12 have been cancelled. Thus, claims 1, 3-5, 13-21 remain pending in the application. The Examiner's rejections and objections are addressed in part by the above-amendments and are otherwise traversed for the reasons presented below.

THE AMENDMENTS TO THE CLAIMS

Claim 1 has been amended specify that R^1 is chosen from the group consisting of indolyl, indazolyl, isoxazolyl, quinolyl, thiazolyl, carbazolyl, thiadiazolyl,benzotriazolyl, benzothiazolyl, and benzimidazolyl and that R^2 is benzoxazolyl or benzothiazolyl. Claim 1 has also been amended to clarify that R^1, R^2, and R^{17} are optionally substituted with 1 to 3 substituents selected from alkyl, hydroxy, alkoxy, halogen, halogen substituted alkyl, phenyl, and phenyl substituted with acetyl, alkyl, alkoxy, hydroxy, halogen, or CF_3. Support for this amendment is found throughout the specification.

Claims 6-11 have been cancelled as drawn to non-elected subject matter

Claim 12 has been cancelled to remove the redundancy resulting from the amendment to claim 1and claims 13-17 have been amended to correctly depend from claim 1.

It is noted that the cancellation of claims 6-12 is without prejudice, without intent to abandon and previously claimed subject matter, and without intent to acquiesce in any rejection of record.

No new matter has been added.

REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has rejected claims 1, 3-5, 12 and 18-21under 35 U.S.C. §112, first paragraph, first paragraph, as failing to comply with the enablement requirement. The Examiner has raised three separate grounds for the rejection, one relating to the inclusion of the terms "acetyl" and "halogen substituted alkyl" in the claims, one relating to the definition of "substituted phenyl" for the R^{17} moiety, and one relating to the scope of the R^1 and R^2 heteroaryl moieties.

With respect to the first and second basis for rejection, Applicants submit that the objected to terms are no longer in the claims and that the Examiner's concerns regarding the optional substitutions on the R^{17} have been fully addressed. The definition of "substituted phenyl" in the R^{17} moiety has been amended to specify that R^{17} may be optionally substituted with 1 to 3 substituents selected from alkyl, hydroxy, alkoxy, halogen, halogen substituted alkyl, phenyl, and phenyl substituted with acetyl, alkyl, alkoxy, hydroxy, halogen, or CF_3. As such, this aspect of the rejection is now moot.

With respect to the third basis for rejection, the R^1 and R^2 moieties, independent claim 1 now recites disubstituted piperazine compounds having terminal R^1 moieties that are chosen from the group consisting of indolyl, indazolyl, isoxazolyl, quinolyl, thiazolyl, carbazolyl, thiadiazolyl, benzotriazolyl, benzothiazolyl, and benzimidazolyl. Similarly, the R^2 moiety is now specified to be either benzoxazolyl or benzothiazolyl. Although Applicants do not agree with the Examiner's opinion regarding the level of enabling disclosure in the specification, in the interest of expediting prosecution, Applicants have

amended the R^1 and R^2 substituents to the currently recited moieties as these groups correspond to those specifically taught in the Examples.

Reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is in order and is respectfully requested.

THE OBJECTION TO THE CLAIMS

The Examiner has indicated that claims 13-17 are objected to, but would be allowable if rewritten in independent form. Applicants respectfully submit that the above amendments and accompanying remarks render the claim objections moot, and all claims are now in a condition for allowance.

THE IDS OF 6/15/04

The IDS submitted on June 15, 2004, disclosed the following references:

U.S. PATENT DOCUMENTS		
Document No.	Issue Date or Publication Date	Name of Patentee or Applicant
U.S. Patent No. 4,588,129	12-10-1985	Kluge et al.
U.S. Patent No. 4,567,264	1-28-1986	Kluge et al.
U.S. Patent No. 4,766,125	8-23-1988	Van Daele et al.
U.S. Patent No. 5,472,707	12-5-1995	Samuels et al.
U.S. Patent No. 5,506,229	4-9-96	Dow et al.
U.S. Patent No. 5,906,988	5-0-1999	Dow
U.S. Patent No. 6,451,798	9-17-2002	Varkhedkar et al.
U.S. Patent No. 6,552,023	04-22-2003	Zablocki et al.
U.S. Patent No. 6,573,264	6-3-2003	Zablocki et al.
U.S. Patent No. 6,677,336	2-7-2002	Zablocki et al.
U.S. Patent No. 6,638,970	10-28-2003	Elzein et al.
U.S. Patent No. 6,677,343	1-13-04	Blackburn et al.
US 2003/0181352	9-25-2003	Ibrahim et al.

FOREIGN PATENT DOCUMENTS		
Document No.	Publication Date	Country
0 407 780	Jan., 1991	EP.
0 483 392	June, 1992	EP.
WO 01/62749	Aug., 2001	WO.
03 141258 A	June, 1991	JP

NONPATENT DOCUMENTS
McCormick, et al. "Ranolazine: A Novel Metabolic Modulator for the Treatment of Angina", Gen Pharmac., vol. 30, No. 5, pp. 639-645, (1998).
Suzuki T et al: "Structure-activity relationship of newly synthesized quinoline derivatives for reversal of multidrug resistance in cancer.", Journal of Chemistry, vol. 40, no. 13, 1997, pages 2047-2052, XP000924067, the whole document, particularly page 2049, table 2, compound 5
Zacharowski K et al: "Ranolazine, a partial fatty acid oxidation inhibitor, reduces myocardial infarct size and cardiac troponin T release in the rat." European Journal of Pharmacology, vol. 418, no. 1-2, April 20, 2001, pages 105-110, XP002215620, the whole document
Lopaschuk G D: "Treating ischemic heart disease by pharmacologically improving cardiac energy metabolism", The American Journal of Cardiology, vol. 82, no. 5A, September 3, 1997, pages 14K-17K, XP002215621, the whole document

As the subject application was filed after June 30, 2003, copies of the U.S. patents and/or publications disclosed in the Information Disclosure Statement are not required and, therefore, were not included with the IDS. Copies of the other references accompany this response.

It is noted that a typographical error was made in the identification of the European Patent 0 483 392. The correct EU patent number is **0 483 392**. Applicants ask that the Examiner correct the 1449 to correctly identify the patent prior to initialing and returning the form to Applicants.

CONCLUSION

For the foregoing reasons, Applicants submit that the claims are in condition for allowance. A Notice of Allowance is requested, and a prompt mailing thereof would be much appreciated.

Should the Examiner have any questions, she is invited to contact the undersigned attorney at (650) 384-8755.

Respectfully submitted,

Date: May 31, 2006

By: _____

J. Elin Hartrum
Reg. No. 43,663
Customer No. 27716

CV Therapeutics, Inc.
3172 Porter Drive
Palo Alto, CA 94304
Phone: (650) 384-8755
Fax: (650) 475-0359

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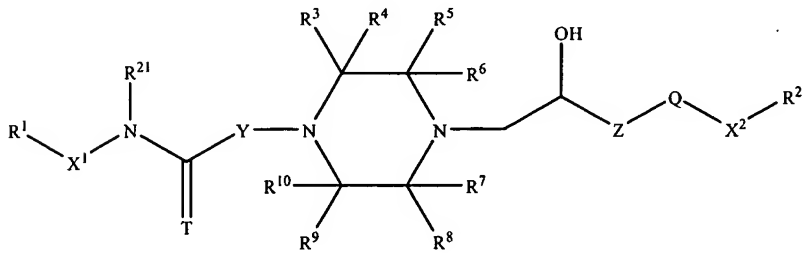
APPENDIX A

CLEAN COPY OF CLAIMS AS AMENDED HEREIN

1. A compound of the formula:



wherein:

R^1 is chosen from the group consisting of indolyl, indazolyl, isoxazolyl, quinolyl, thiazolyl, carbazolyl, thiadiazolyl,benzotriazolyl, benzothiazolyl, and benzimidazolyl optionally substituted with 1 to 3 substituents selected from acetyl, alkyl, hydroxy, alkoxy, halogen, halogen substituted alkyl, phenyl, and phenyl substituted with alkyl, alkoxy, hydroxy, halogen, or CF_3;

R^2 is benzoxazolyl or benzothiazolyl optionally substituted with 1 to 3 substituents selected from alkyl, hydroxy, alkoxy, halogen, halogen substituted alkyl, phenyl, and phenyl substituted with acetyl, alkyl, alkoxy, hydroxy, halogen, or CF_3;

X^1 is a covalent bond, or $-(CR^{15}R^{16})_p-$, in which R^{15} and R^{16} are independently hydrogen, hydroxy, lower alkyl, or $-C(O)OR^{17}$, in which R^{17} is hydrogen, lower alkyl, phenyl, or phenyl substituted with alkyl, alkoxy, hydroxy, halogen, or CF_3, and p is 1, 2 or 3; with the proviso that when p is 1, R^{15} and R^{16} cannot be hydroxy;

R^{21} is hydrogen or lower alkyl;

T is oxygen or sulfur;

Y and Z are $-(CR^{18}R^{19})_q-$ and q at each occurrence is 1, 2 or 3, in which R^{18} and R^{19} at each occurrence is hydrogen or lower alkyl; and

R^3, R^4, R^5, R^6, R^7, R^8, R^9, and R^{10} at each occurrence are hydrogen, lower alkyl, or -C(O)R; in which R is $-OR^{11}$ or $-NR^{11}R^{12}$, where R^{11} and R^{12} are hydrogen or lower alkyl; or

R^3 and R^4, R^5 and R^6, R^7 and R^8, R^9 and R^{10}, when taken together with the carbon to which they are attached, represent carbonyl;

Q is oxygen, sulfur, or $-NR^{20}-$, in which R^{20} is hydrogen or optionally substituted lower alkyl;

X^2 is a covalent bond or $-(CR^{18}R^{19})_q-$ wherein q at each occurrence is 1, 2 or 3, and R^{18} and R^{19} at each occurrence is hydrogen or lower alkyl; and with the proviso that when X^1 is a covalent bond and Y is $-(CR^{18}R^{19})_q-$ in which q is 1 and R^{18} and R^{19} are hydrogen, then R^1 is not optionally substituted phenyl.

3. The compound of claim 1, wherein R^3, R^4, R^6, R^7, R^8, R^9, and R^{10} at each occurrence are hydrogen and R^5 is hydrogen or methyl.

4. The compound of claim 3, wherein Q and T are both oxygen and X^2 is a covalent bond.

5. The compound of claim 4, wherein R^{21} is hydrogen, Y is methylene or ethylene, and Z is methylene.

13. The compound of claim 1, wherein R^1 is 4-(4-chlorophenyl)thiazol-2-yl, R^2 is 2-methylbenzothiazol-5-yl, R^5 is hydrogen, and X^1 is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-[4-(4-chlorophenyl)(1,3-thiazol-2-yl)]acetamide.

14. The compound of claim 1, wherein R^1 is 4-(4-chlorophenyl)thiazol-2-yl, R^2 is 2-methylbenzothiazol-5-yl, R^5 is methyl, and X^1 is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]-3-methylpiperazinyl}-N-[4-(4-chlorophenyl)(1,3-thiazol-2-yl)]acetamide.

15. The compound of claim 1, wherein R^1 is 9-ethylcarbazol-3-yl, R^2 is 2-methylbenzothiazol-5-yl, R^5 is hydrogen, and X^1 is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-(9-ethylcarbazol-3-yl)acetamide.

16. The compound of claim 1, wherein R^1 is 6-quinolyl, R^2 is 2-phenylbenzoxazol-5-yl, R^5 is hydrogen, and X^1 is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-phenylbenzoxazol-5-yloxy)propyl]piperazinyl}-N-(6-quinolyl)acetamide.

17. The compound of claim 1, wherein R^1 is 8-quinolyl, R^2 is 2-methylbenzothiazol-5-yl, R^5 is hydrogen, and X^1 is a covalent bond, namely 2-{4-[(2R)-2-hydroxy-3-(2-methylbenzothiazol-5-yloxy)propyl]piperazinyl}-N-(8-quinolyl)acetamide.

18. A method of treating a disease state chosen from diabetes, damage to skeletal muscles resulting from trauma or shock and a cardiovascular disease selected from the group consisting of atrial arrhythmia, intermittent claudication, ventricular arrhythmia, Prinzmetal's (variant) angina, stable angina, unstable angina, congestive heart disease, and myocardial infarction in a mammal by administration of a therapeutically effective dose of a compound of claim 1.

19. The method of claim 18, wherein the disease state is a cardiovascular disease selected from atrial arrhythmia, intermittent claudication, ventricular arrhythmia, Prinzmetal's (variant) angina, stable angina, unstable angina, congestive heart disease, and myocardial infarction.

20. The method of claim 18, wherein the disease state is diabetes.

21. A pharmaceutical composition comprising at least one pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 1.